Novel screening tests for liver cancer

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New data from two clinical trials presented today at the International Liver Congress 2013 demonstrate substantial improvements in the detection of both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC) using diagnostic urine tests.

HCC is common throughout the world and most often develops as a late complication of chronic viral hepatitis or cirrhosis of any cause. The overall survival rate of HCC is poor and so screening for HCC offers the best hope for early detection, eligibility for treatment, and improved survival. While effective therapies exist, the available screening tests to detect HCC – alpha-fetoprotein (AFP) and ultrasound – are reported to have low sensitivity and specificity (50–85% and 70–90%, respectively).

Preliminary data demonstrate the performance of urinary metabolites in helping to diagnose HCC. Urine samples were collected from four subject groups in West Africa on the case-control platform of PROLIFICA 'Prevention of Liver Fibrosis and Carcinoma in Africa' as follows: patients with HCC (n=65), cirrhosis (Cir, n=36), non-cirrhotic liver disease (DC, n=110) and healthy controls (NC, n=91). HCC patients were diagnosed using EASL guidelines.

Multivariate analyses of urinary nuclear magnetic resonance (NMR) spectra showed a distinct profile for urine of patients with HCC compared to Cir, DC and NC with sensitivity of 87%, 86% and 97% respectively. These results suggest that Urinary metabolite profile outperforms serum AFP which only differentiated HCC from these groups by 79% (Cir), 75% (DC) and 76% NC) respectively. The

metabolites that were significantly increased (p

EASL General Secretary, Prof. Mark Thursz commented: "These findings will be welcomed by physicians as they validate urinary metabolic profiling as a potential screening tool for HCC, with superior diagnostic accuracy to serum AFP and – if investigated further and put into practice – this non-invasive technique could simplify and improve clinical diagnosis and outcomes for patients."

Similarly, detection of CC remains a diagnostic challenge and physicians will be encouraged by results from a Phase II study showing that a combined bile and urine proteomic test increased diagnostic accuracy of CC in patients with biliary strictures (an abnormal narrowing of the common bile duct) of unknown origin.

Having recently established diagnostic peptide marker models in bile and urine to detect both local and systemic changes during CC progression, investigators combined both models with the aim of reaching a higher diagnostic accuracy.

The data demonstrated this model enables impressive CC-diagnosis with an accuracy of more than 90% that is most applicable for patients with biliary strictures of unknown origin referred to endoscopy.

Prof. Mark Thursz added: "These important findings substantially improve the diagnosis of CC and may lead to early therapy and improved prognosis. Overall both data sets demonstrate the increasing value of proteomic and metabonomic techniques and if confirmed by further investigation, clinicians may soon be using simple urine dip-stick tests to diagnose HCC and CC."

A logistic regression model composed of the bile and urine proteomic classification factors lead to an area under curve (AUC) of 0.96, and

92% sensitivity and 84% specificity at the best cut-off. Only three of the 36 CC patients were false negative and two of the 33 PSC patients were false positive classified. Inclusion of CA19-9 and bilirubin values to the logistic regression model was of minor benefit.

Cholangiocarcinoma or bile duct cancer is rare and almost always adenocarcinoma which starts in the lining of the bile duct. The cause of most cholangiocarcinomas is unknown but people with chronic inflammatory bowel conditions or congential abnormalities of the bile duct have a higher risk of developing the cancer.

More information: References:

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